

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

HIRAYAMA, Kouji, et al.

Continuation of

U.S. Appln. No.: 08/726,170

Group Art Unit: Not yet Assigned

Confirmation No.: Not yet Assigned

Examiner: Not yet Assigned

Filed: August 17, 2001

For: TEST APPARATUS FOR ASSAYING A COMPONENT IN A LIQUID SAMPLE

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-identified application as follows:

IN THE SPECIFICATION:

Amend the specification by inserting before the first line the sentence:

CROSS REFERENCE TO RELATED APPLICATIONS

This is a Continuation of Application No. 08/726,170 filed October 4, 1996, the disclosure of which is incorporated herein by reference.

On page 1, please replace the first paragraph with the following paragraph:

The present invention relates to a test apparatus which is used for assaying a specific component contained in a liquid sample, especially a blood sample such as whole blood and serum, and a body fluid such as urine and cerebrospinal fluid by a color reaction. More particularly, the present invention relates to a test apparatus using reflected light as a measuring means.

PRELIMINARY AMENDMENT

Continuation of U.S. Appln. No. 08/726,170

On page 1, please replace the second paragraph with the following paragraph:

In order to measure a specific component in a liquid sample quickly and simply, for example, glucose, cholesterol or the like in a blood sample, or glucose, hemoglobin or the like in a body fluid sample, a dry type test apparatus comprises a support having thereon a reagent layer containing at least a reagent capable of developing a color by a reaction with the specific component.

On page 2, please replace the first full paragraph with the following paragraph:

Test apparatuses using reflected light can be divided roughly into two types from the viewpoint of sample supply to the reagent layer; one is a test apparatus having a sample-supplying area and a detecting area (namely, an incident light side area) on the same side, and another is a test apparatus having a sample-supplying area and a detecting area on different sides.

On page 5, please replace the second full paragraph with the following paragraph:

In order to resolve the above problems, the inventors of the present invention have conducted intensive studies and found that the influence of unnecessary reflected light can be avoided when an area which has substantially no influence on the reflected light at a measured wavelength is provided on one side of a reagent layer opposite to the side where the light is incident, because the reflection of light passed through a reflection layer in the reagent layer is lowered in that area.

On page 6, please replace the paragraph beginning at line 8 with the following paragraph:

wherein at least a portion of said cover covering the detecting area is of a color which substantially has no influence on said reflected light at a measured wavelength.

On page 6, please replace the paragraph bridging pages 6 and 7 with the following paragraph:

The test apparatus for use in the present invention can have the following embodiments. One of them is a test apparatus having the same basic structure disclosed in JP-A-4-188065, in which its cover is fixed on a support in such a manner that a sample-holding room is formed between the reagent layer and the cover which has a sample-supplying hole and an air exhaust hole. This cover is of a color which substantially has no influence on the reflected light at a measured wavelength (see sectional views of Figs. 1 and 2, Fig. 2 is an expanded view of the reagent layer and its surrounding area of Fig. 1).

On page 7, please replace the first full paragraph with the following paragraph:

When this test apparatus is used, a liquid sample is added dropwise through the sample-supplying hole. The thus added liquid sample flows in the sample-holding room and reaches the reagent layer set at a halfway position of the sample holding room. When the sample is whole blood, blood plasma alone is separated by the blood cell separating action in the reagent layer, and reacts with the reagent in a porous membrane which acts as a sample-holding layer.

On page 7, please replace the fourth paragraph with the following paragraph:

PRELIMINARY AMENDMENT
Continuation of U.S. Appln. No. 08/726,170

When this test apparatus is used, a liquid sample is spotted on position A of the reagent layer. Thereafter, the liquid sample flows into in the reagent layer and is mixed therewith, and a reaction of blood plasma with the reagent occurs in the porous membrane which acts as a sample-holding layer. That is, the porous membrane of the test apparatus also acts as a matrix to transport the liquid sample.

On page 8, please replace the third paragraph with the following paragraph:

The porous membrane may be provided between the reagent layer and the support. However, the porous membrane is merely a base which is effective in holding a necessary portion of liquid sample for carrying out the reaction and in coating the reagent on a layer. Accordingly, it is not particularly necessary for the construction of the present invention. Examples of the porous membrane for use in the present invention include polypropylene film (e.g., Celgard produced by Hoechst), polysulfone film (e.g., Filterite produced by Memtec), and polycarbonate film (e.g., Cyclopore produced by Whatman).

On page 8, please replace the paragraph bridging pages 8 and 9 with the following paragraph:

In the test apparatus of the present invention, it is preferable to form a light reflection layer on the reagent layer in order to facilitate observation of the coloring situation with the naked eye and to improve detection sensitivity by increasing the amount of light in the detecting area. With regard to properties and size of the light reflection layer, it is preferable to use such a thin and simple layer that it does not react with the reagent to be used in the reagent layer and with liquid samples, does not inhibit coloration of the reagent layer and can minimize its influence upon a

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

permeation rate of liquid samples. Examples of the light reflective particles include titanium dioxide, magnesium oxide, and barium sulfate. They may be used alone, or polymer beads containing them may be used.

On page 9, please replace the second paragraph with the following paragraph:

As described in the foregoing, unnecessary light passes through the light reflection layer when the light reflection layer is thinned in order to maintain a permeation rate of liquid samples. However, it is not necessary to take such unnecessary light into consideration in the present invention. In consequence, the reflection layer can be made into a simple structure (namely a thin layer) in order to increase the permeation rate of liquid samples, and a shortened measuring period can be expected because of the apparent increase in the liquid sample permeation rate. As an example of the reflection layer having a simple structure, the reagent layer and light reflection layer may be made into one body by kneading light reflective particles in the reagent layer, thereby adding light reflection function to the reagent layer itself.

On page 11, please replace the paragraph beginning at line 2 with the following paragraph:

Examples of methods for preparing the cover are shown in the following.

On page 13, please replace the first paragraph with the following paragraph:

The thus prepared apparatus of porous film, with its reagent layer up was put on a support made of PET and coated with a thermoplastic resin (1 in Fig. 1) having a through hole of 4 mm in diameter (11 in Fig. 1) and then adhered to the support by thermo-compression bonding. A cover which was made of ABS resin and molded in a

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

black color (reflectance: 5.3%, 5 in Fig. 1) was also put on the resulting support with its PET side downward and adhered by thermo-compression bonding, in order to cover the reagent and form a sample-holding room (4 in Fig. 1) between the cover and the support, thereby obtaining a test apparatus.

On page 13, please replace the second paragraph with the following paragraph:

Since the cover (5 in Fig. 1) has a sample-supplying hole (51 in Fig. 1) and an air exhaust hole (52 in Fig. 1), a liquid sample added dropwise through the sample-supplying hold advances by capillary action and gravity flow action, getting over the reagent layer and wetting it. A portion of the sample reacted with the reagents enters into the porous film and is held therein.

On page 15, please replace the second paragraph with the following paragraph:

Even when the values obtained with the hematocrit values of 0% and 65% , which rarely occur in reality, were excluded, fluctuations between maximum and minimum values of the reflectance and K/S value were found to be 0.3% or 0.6% and 0.017 or 0.035, respectively, when the test apparatus of the present invention was used; on the other hand, such fluctuations were 2.0% and 0.083 when the control test apparatus was used.

On page 16, please replace the first paragraph with the following paragraph:

Thus, as has been described in the foregoing, since the test apparatus of the present invention is not influence by unnecessary light reflected into the cover passing through the reflection layer in the reagent layer, the problem of fluctuation of the

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

measured values due to difference in color of respective liquid samples can be resolved.

IN THE CLAIMS:

Please cancel claims 1-10 without prejudice or disclaimer.

Please add the following new claims:

11. (new) A test apparatus for assaying a component in a liquid sample by measuring a reflected light, comprising:

a support defining an upper side and a lower side and having one of a through hole and a light permeable area,

a reagent layer defining an upper side and a lower side and having a detecting area, the reagent layer being fixed on the upper side of the support to cover one of the through hole and light permeable area, and

a cover including a lower side facing the reagent layer and which covers at least the detecting area,

wherein at least a portion of said cover covering the detecting area is of a color which one of reflects an amount of light at a measured wavelength, and fully absorbs light at a measured wavelength, such that said color has substantially no influence on the reflected light at the measured wavelength;

wherein said color is black; and

wherein said reflected light is measured from the lower side of both the reagent layer and the cover.

12. (New) The test apparatus as claimed in claim 11, wherein said cover is fixed on the support in such a manner that a gap exists between the cover and the reagent

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

layer, and said cover has a sample-supplying hole and an air exhaust hole.

13. (New) The test apparatus as claimed in claim 11, wherein said cover contacts one side of the reagent layer opposite to the support.

14. (New) The test apparatus as claimed in claim 11, further comprising a light reflection layer in contact with the reagent layer.

15. (New) The test apparatus as claimed in claim 11, wherein said reagent layer comprises light reflective particles.

16. (New) The test apparatus as claimed in claim 11, wherein the liquid sample is whole blood and said reagent is responsive to a component of said blood.

17. (New) The test apparatus as claimed in claim 11, further comprising a porous membrane disposed between the reagent layer and the support.

IN THE ABSTRACT:

Please delete the present Abstract of the Disclosure and replace it with the following new Abstract of the Disclosure.

A test apparatus for assaying a component in a liquid sample by measuring a reflected light, comprising a support having a through hole or a light permeable area, a reagent layer having a detecting area fixed on the support to cover said through hole or light permeable area, and a cover which covers at least the detecting area, wherein at least a portion of the cover covering the detecting area is of a color which substantially has no influence on the reflected light at a measured wavelength.

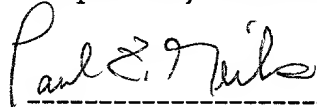
PRELIMINARY AMENDMENT
Continuation of U.S. Appln. No. 08/726,170

REMARKS

Claims 11-17 are all the claims pending in this application. Support for claims 11-17 can be found, for example, in original claim 1 and on page 6, lines 22-25; page 7, line 8 and lines 14-16; page 8, lines 13-14 and lines 24-26; page 9, lines 9-11 and page 13, line 6.

Entry and consideration of this Amendment is respectfully requested.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

Before the first paragraph, the following is inserted.

--CROSS REFERENCE TO RELATED APPLICATIONS

This is a Continuation of Application No. 08/726,170 filed October 4, 1996, the disclosure of which is incorporated herein by reference.--

On page 1, the first paragraph:

The present invention relates to a test apparatus which [are] is used for assaying a specific component contained in a liquid sample, especially a blood sample such as whole blood and serum, and a body fluid such as urine and cerebrospinal fluid by a color reaction. More particularly, the present invention relates to a test apparatus using reflected light as a measuring means.

On page 1, the second paragraph:

In order to measure a specific component in a liquid sample quickly and simply, for example, glucose, cholesterol or the like in a blood sample, or glucose, hemoglobin or the like in a body fluid sample, a dry type test apparatus [comprising] comprises a support having [provided] thereon a reagent layer containing at least a reagent capable of developing a color by a reaction with the specific component.

On page 2, the first full paragraph:

[The test] Test apparatuses using [the] reflected light can be divided roughly into two types from the viewpoint of sample supply to the reagent layer; one is a test

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

apparatus having a sample-supplying area and a detecting area (namely, an incident light side area) on the same side, and another is a test apparatus having a sample-supplying area and a detecting area on different sides.

On page 5, the second full paragraph:

In order to resolve the above problems, the inventors of the present invention have conducted intensive studies and found that the influence of unnecessary [reflection] reflected light can be avoided when an area which has substantially [having] no influence on the reflected light at a measured wavelength is provided on one side of a reagent layer opposite to the side where the [of] light is incident [direction], because the reflection of light passed through a reflection layer in the reagent layer is lowered in that [the] area.

On page 6, the paragraph beginning at line 8:

wherein at least a portion of said cover covering the detecting area [in said cover] is of [processed into] a color which substantially has no influence on said reflected light at a measured wavelength.

On page 6, the paragraph bridging pages 6 and 7:

The test apparatus for use in the present invention can have the following embodiments. One of them is a test apparatus having the same basic structure disclosed in JP-A-4-188065, in which its cover is fixed on a support in such a manner that a sample-holding room is formed between the reagent layer and the cover which has a sample-supplying hole and an air exhaust hole. This cover is of [processed into] a color which substantially has no influence on the reflected light at a measured

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

wavelength (see sectional views of Figs. 1 and 2, Fig. 2 is an expanded view of the reagent layer and its surrounding area of Fig. 1).

On page 7, the first full paragraph:

When this test apparatus is used, a liquid sample is added dropwise through the sample-supplying hole. The thus added liquid sample flows [develops] in the sample-holding room and reaches the reagent layer set at a halfway position of the sample holding room. When the sample is whole blood, blood plasma alone is separated by the blood cell separating action in the reagent layer, and reacts with the reagent in a porous membrane which acts as a sample-holding layer.

On page 7, the fourth paragraph:

When this test apparatus is used, a liquid sample is spotted on position A of the reagent layer. Thereafter, the liquid sample flows into [develops] in the reagent layer and is mixed therewith, and a reaction of blood plasma with the reagent occurs in the porous membrane which acts as a sample-holding layer. That is, the porous membrane of the test apparatus also acts as a matrix to transport the liquid sample.

On page 8, third paragraph:

The porous membrane may be provided between the reagent layer and the support. However, the porous membrane is merely a base which is effective in holding a necessary portion of liquid sample for carrying out the reaction and in coating the reagent on [in] a layer. Accordingly, it is not particularly necessary for the construction of the present invention. Examples of the porous membrane for use in the present invention include polypropylene film (e.g., Celgard produced by Hoechst),

PRELIMINARY AMENDMENT
Continuation of U.S. Appl. No. 08/726,170

polysulfone film (e.g., Filterite produced by Memtec), and polycarbonate film (e.g., Cyclopore produced by Whatman).

On page 8, the paragraph bridging pages 8 and 9:

In the test apparatus of the present invention, it is preferable to form a light reflection layer on the reagent layer in order to facilitate observation of the coloring situation with the naked eye and to improve detection sensitivity by increasing the amount of light in the detecting area. With regard to properties and size of the light reflection layer, it is preferable to use such a thin and simple layer that it does not react with the reagent to be used in the reagent layer and with liquid samples, does not inhibit coloration of the reagent layer and can minimize its influence upon a permeation rate of liquid samples [as small as possible]. Examples of the light reflective particles include titanium dioxide, magnesium oxide, and barium sulfate. They may be used alone, or polymer beads containing them may be used.

On page 9, the second paragraph:

As described in the foregoing, unnecessary light passes through the light reflection layer when the light reflection layer is thinned in order to maintain [ensure] a permeation rate of liquid samples. However, it is not necessary to take such unnecessary light into consideration in the present invention. In consequence, the reflection layer can be made into a simple structure (namely a thin layer) in order to increase the [a] permeation rate of liquid samples, and a shortened measuring period can be expected because of the apparent increase in the liquid sample permeation rate. As an example of the reflection layer having a simple structure, the reagent layer and

PRELIMINARY AMENDMENT

Continuation of U.S. Appl. No. 08/726,170

light reflection layer may be made into one body by kneading light reflective particles in the reagent layer, thereby adding light reflection function to the reagent layer itself.

On page 11, the paragraph beginning at line 2:

Examples of [method] methods for preparing the cover are shown in the following.

On page 13, the first paragraph:

The thus prepared apparatus of porous film, with its reagent layer up [being upside,] was put on a support made of PET and coated with a thermoplastic resin (1 in Fig. 1) having a through hole of 4 mm in diameter (11 in Fig. 1) and then adhered to the support by thermo-compression bonding. A cover which was made of ABS resin and molded in a black color (reflectance: 5.3%, 5 in Fig. 1) was also [further] put on the resulting support with [by setting] its PET side downward and adhered by thermo-compression bonding, in order to cover the reagent and form a sample-holding room (4 in Fig. 1) between the cover and the support, thereby obtaining a test apparatus.

On page 13, the second paragraph:

Since the cover (5 in Fig. 1) has a sample-supplying hole (51 in Fig. 1) and an air exhaust hole (52 in Fig. 1), a liquid sample added dropwise through the sample-supplying hold [develops and] advances by [the] capillary action and gravity flow action, getting over the reagent layer and wetting it. A portion of the sample reacted with the reagents enters into the porous film and is held therein.

On page 15, the second paragraph:

Even when the values obtained with the hematocrit values of 0% and 65% , which rarely [seemed hardly to] occur in reality, were excluded, fluctuations between

PRELIMINARY AMENDMENT
Continuation of U.S. Appln. No. 08/726,170

maximum and minimum values of the reflectance and K/S value were found to be 0.3% or 0.6% and 0.017 or 0.035, respectively, when the test apparatus of the present invention was used; on the other hand, such fluctuations were 2.0% and 0.083 when the control test apparatus was used.

On page 16, the first paragraph:

Thus, as has been described in the foregoing, since the test apparatus of the present invention is not influence by unnecessary light reflected into the cover passing through the reflection layer in the reagent layer, the problem of [causing] fluctuation of the measured values due to difference in color of respective liquid samples can be resolved.

IN THE CLAIMS:

Claims 11-17 have been added as new claims.

IN THE ABSTRACT OF DISCLOSURE:

The abstract is changed as follows:

A test apparatus for assaying a component in a liquid sample by measuring a reflected light, comprising a support having a through hole or a light permeable area, a reagent layer having a detecting area fixed on the support to cover said through hole or light permeable area, and a cover which covers at least the detecting area, wherein at least a portion of the cover covering the detecting area [in the cover] is of [process into] a color which substantially has no influence on the reflected light at a measured wavelength.